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**A home away from home: challenges and opportunities in engineering in vitro muscle satellite cell niches.**

**Journal:** Differentiation

**Publication Year:** 2009

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**PubMed link:** 19751902

**Funding Grants:** Regulation of Stem Cell Fate in Bioengineered Arrays of Hydrogel Microwells

**Public Summary:**

**Scientific Abstract:**

Satellite cells are skeletal muscle stem cells with a principal role in postnatal skeletal muscle regeneration. Satellite cells, like many tissue-specific adult stem cells, reside in a quiescent state in an instructive, anatomically defined niche. The satellite cell niche constitutes a distinct membrane-enclosed compartment within the muscle fiber, containing a diversity of biochemical and biophysical signals that influence satellite cell function. A major limitation to the study and clinical utility of satellite cells is that upon removal from the muscle fiber and plating in traditional plastic tissue culture platforms, their muscle stem cell properties are rapidly lost. Clearly, the maintenance of stem cell function is critically dependent on in vivo niche signals, highlighting the need to create novel in vitro microenvironments that allow for the maintenance and propagation of satellite cells while retaining their potential to function as muscle stem cells. Here, we discuss how emerging biomaterials technologies offer great promise for engineering in vitro microenvironments to meet these challenges. In engineered biomaterials, signaling molecules can be presented in a manner that more closely mimics cell-cell and cell-matrix interactions, and matrices can be fabricated with diverse rigidities that approximate in vivo tissues. The development of in vitro microenvironments in which niche features can be systematically modulated will be instrumental not only to future insights into muscle stem cell biology and therapeutic approaches to muscle diseases and muscle wasting with aging, but also will provide a paradigm for the analysis of numerous adult tissue-specific stem cells.

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